In another embodiment, a therapeutic procedure comprises attaching a porphyrin or photodynamic therapy agent to a bioconjugate, and then administering light of an appropriate wavelength for detecting and treating an abnormality.

The compositions of the invention can be formulated for enteral or parenteral administration. These formulations contain an effective amount of the dye-biomolecule conjugate along with conventional pharmaceutical carriers and excipients appropriate for the type of administration contemplated. For example, parenteral formulations advantageously contain a sterile aqueous solution or suspension of the inventive conjugate, and may be injected directly, or may be mixed with a large volume parenteral composition or excipient for systemic administration as is known to one skilled in the art. These formulations may also contain pharmaceutically acceptable buffers and/or electrolytes such as sodium chloride.

Formulations for enteral administration may vary widely, as is well known in the art. In general, such formulations are aqueous solutions, suspensions or emulsions which contain an effective amount of a dye-biomolecule conjugate. Such enteral compositions may include buffers, surfactants, thixotropic agents, and the like. Compositions for oral administration may also contain flavoring agents and other ingredients for enhancing their organoleptic qualities.

The inventive compositions of the carbocyanine dye bioconjugates for diagnostic uses are administered in doses effective to achieve the desired effect. Such doses may vary widely, depending upon the particular conjugate employed, the organs or tissues which are the subject of

the imaging procedure, the imaging equipment being used, and the like. The compositions may be administered either systemically, or locally to the organ or tissue to be imaged, and the patient is then subjected to diagnostic imaging and/or therapeutic procedures.

The present invention is further detailed in the following Examples, which are offered by way of illustration and are not intended to limit the scope of the invention in any manner.

Example 1

Synthesis of Indocyaninebispropanoic acid Dye (Figure 1A, n = 1)

A mixture of 1,1,2-trimethyl-[1H]-benz[e]indole (9.1 g, 43.58 mmoles) and 3-bromopropanoic acid (10.0 g, 65.37 mmoles) in 1,2-dichlorobenzene (40 ml) was heated at 110 °C for 12 hours. The solution was cooled to ambient temperature. The red residue obtained was filtered and washed with acetonitrile:diethyl ether (1:1$^{v/v}$) mixture. The solid obtained was dried at ambient temperature under vacuum to give 10 g (64%) of light brown powder.

A portion of this solid (6.0 g; 16.56 mmoles), glutaconic aldehyde dianilide hydrochloride (Lancaster Synthesis, Windham, NH) (2.36 g, 8.28 mmoles), and sodium acetate trihydrate (2.93 g, 21.53 mmoles) in ethanol (150 ml) were refluxed for 90 minutes. After evaporating the solvent, 40 ml of a 2 N aqueous HCl was added to the residue. The mixture was centrifuged and the supernatant was decanted. This procedure was repeated until the supernatant became nearly colorless. About 5 ml of a water:acetonitrile (3:2$^{v/v}$) mixture was added to the solid residue and lyophilized to obtain 2 g of dark green flakes. The purity of the compound was established with ^{1}H-nuclear magnetic

resonance (^{1}H-NMR) and liquid chromatography/mass spectrometry (LC/MS) as is known to one skilled in the art.

Example 2

Synthesis of Indocyaninebishexanoic acid Dye (Figure 1A, n = 4)

A mixture of 1,1,2-trimethyl-[1H]-benz[e]indole (20 g, 95.6 mmoles) and 6-bromohexanoic acid (28.1 g, 144.1 mmoles) in 1,2-dichlorobenzene (250 ml) was heated at 110 C for 12 hours. The green solution was cooled to ambient temperature and the brown solid precipitate that formed was collected by filtration. After washing the solid with 1,2-dichlorobenzene and diethyl ether, the brown powder obtained (24 g, 64%) was dried under vacuum at ambient temperature. A portion of this solid (4.0 g; 9.8 mmoles) glutacoaldehyde dianil monohydrochloride (1.4 g, 5 mmoles) and sodium acetate trihydrate (1.8 g, 12.9 mmoles) in ethanol (80 ml) were refluxed for 1 hour. After evaporating the solvent, 20 ml of 2 N aqueous HCl was added to the residue. The mixture was centrifuged and the supernatant was decanted. This procedure was repeated until the supernatant became nearly colorless. About 5 ml of a water:acetonitrile (3:2$^{v/v}$) mixture was added to the solid residue and lyophilized to obtain about 2 g of dark green flakes. The purity of the compound was established with ^{1}H-NMR and LC/MS.

Example 3

Synthesis of Peptides

Peptides of this invention were prepared by similar procedures with slight modifications in some cases.

Octreotate, an octapeptide, has the amino acid sequence D-Phe-Cys'-Tyr-D-Trp-Lys-Thr-Cys'-Thr (SEQ ID NO:1), wherein Cys' indicates the